

*National Institute  
of Mental Health*

*Decade of the Brain*

# Alzheimer's Disease

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of Mental Health

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# **Message from the National Institute of Mental Health**

Research conducted and supported by the National Institute of Mental Health (NIMH) brings hope to millions of people who suffer from mental illness and to their families and friends. In many years of work with animals as well as human subjects, researchers have advanced our understanding of the brain and vastly expanded the capability of mental health professionals to diagnose, treat, and prevent mental and brain disorders.

Now, in the 1990s, which the President and Congress have declared "The Decade of the Brain," we stand at the threshold of a new era in brain and behavioral sciences. Through research we will learn even more about mental disorders such as depression, manic-depressive illness, schizophrenia, panic disorder, and obsessive-compulsive disorder. And we will be able to use this knowledge to develop new therapies that can help more people overcome mental illness.

The National Institute of Mental Health is part of the National Institutes of Health (NIH), the Federal Government's primary agency for biomedical and behavioral research. NIH is a component of the U.S. Department of Health and Human Services.

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"Alzheimer's disease" is the term used to describe a dementing disorder marked by certain brain changes, regardless of the age of onset. Alzheimer's disease is not a normal part of aging—it is not something that inevitably happens in later life. Rather, it is one of the dementing disorders, a group of brain diseases that lead to the loss of mental and physical functions. The disorder, whose cause is unknown, affects a small but significant percentage of older Americans. A very small minority of Alzheimer's patients are under 50 years of age. Most are over 65.

Alzheimer's disease is the exception, rather than the rule, in old age. Only 5 to 6 percent of older people are afflicted by Alzheimer's disease or a related dementia—but this means approximately 3 to 4 million Americans have one of these debilitating disorders. Research indicates that 1 percent of the population aged 65-74 has severe dementia, increasing to 7 percent of those aged 75-84 and to 25 percent of those 85 or older. At least half the people in U.S. nursing homes have Alzheimer's disease or a related disorder; in 1991, the annual cost of caring for individuals with Alzheimer's disease and related dementias in institutional and community settings was estimated between \$24 billion and \$48 billion for direct costs alone and is probably higher today. As our population ages and the number of Alzheimer's patients increases, costs of care will rise as well.

Although Alzheimer's disease is not curable or reversible, there are ways to alleviate symptoms and suffering and to assist families. Not every person with this illness must necessarily move to a nursing home. Many thousands of patients—especially those in the early stages of the disease—are cared for by their families in the community. Indeed, one of the most important aspects of medical management is family education and family support services. When, or whether, to transfer a patient to a nursing home is a decision to be carefully considered by the family.

## What is Alzheimer's?

**The main risk factor for Alzheimer's disease is increased age.**

## Who Gets Alzheimer's disease?

The main risk factor for Alzheimer's disease is increased age. The rates of the disease increase markedly with advancing age, with 25 percent of people over 85 suffering from Alzheimer's or other severe dementia.

**The onset of Alzheimer's disease is usually very slow and gradual.**

Some investigators, describing a family pattern of Alzheimer's disease, suggest that in some cases heredity may influence its development. A genetic basis has been identified through the discovery of several genetic markers on chromosomes 21 and 14 for a small subgroup of families in which the disease has frequently occurred at relatively early ages (beginning before age 50). Some evidence points to chromosome 19 as implicated in certain other families that have frequently had the disease develop at later ages.

At the same time, data indicate that the likelihood that a close relative (sibling, child, or parent) of an afflicted individual will develop Alzheimer's disease is low. In most cases, such an individual's risk is only slightly higher than that of someone in the general population, where the lifetime risk is below 1 percent. And, of course, many disorders have a genetic potential that is never expressed—that is, despite being at risk for a certain illness, one might go through life without ever developing any symptom of the disease.

## **What To Expect When Someone Has Alzheimer's Disease**

Mary Ellen's friends thought she was the perfect mother, wife, friend, and hostess. Her husband George, a prolific author, counted on her to edit his work and manage his schedule. He was the first to notice that she was no longer able to remember her good friends' names, her children's birthdays, or the details of her busy life. During social occasions, she could be seen sitting on the sidelines, answering politely but vaguely if spoken to, but never engaged in meaningful conversation. She was no longer able to go shopping or pay the household bills as she had done for the past 30 years. George was bewildered and could not understand what had happened to his close companion of so many years.

The onset of Alzheimer's disease is usually very slow and gradual, seldom occurring before age 65. Over time, however, it follows a progressively more serious course. Among the symptoms that typically develop, none is unique to Alzheimer's disease at its various stages. It is therefore essential for suspicious changes to be thoroughly evaluated

before they become inappropriately or negligently labeled Alzheimer's disease.

Problems of memory, particularly recent or short-term memory, are common early in the course of the disease. For example, the individual may, on repeated occasions, forget to turn off the iron or may not recall which of the morning's medicines were taken. Mild personality changes, such as less spontaneity or a sense of apathy and a tendency to withdraw from social interactions, may occur early in the illness. As the disease progresses, problems in abstract thinking or in intellectual functioning develop. The individual may begin to have trouble with figures when working on bills, with understanding what is being read, or with organizing the day's work. Further disturbances in behavior and appearance may also be seen at this point, such as agitation, irritability, quarrelsomeness, and diminishing ability to dress appropriately.

Later in the course of the disorder, the affected individuals may become confused or disoriented about what month or year it is and be unable to describe accurately where they live or to name correctly a place being visited. Eventually they may wander, be unable to engage in conversation, seem inattentive and erratic in mood, appear uncooperative, lose bladder and bowel control, and, in extreme cases, become totally incapable of caring for themselves if the final stage is reached. Death then follows, perhaps from pneumonia or some other problem that occurs in severely deteriorated states of health. The average course of the disease from the time it is recognized to death is about 6 to 8 years, but it may range from under 2 to over 20 years. Those who develop the disorder later in life may die from other illnesses (such as heart disease) before Alzheimer's disease reaches its final and most serious stage.

Though the changes just described represent the general range of symptoms for Alzheimer's disease, the specific problems, along with the rate and severity of decline, can vary considerably with different individuals. Indeed, most persons with Alzheimer's disease can function at a reasonable level and remain at home far into the course of the disorder. Moreover, throughout much of the course of the illness individuals maintain the capacity for giving and receiving love, for sharing warm interpersonal relationships, and for participating in a variety of meaningful activities with family and friends.

**Most persons with Alzheimer's disease can function at a reasonable level and remain at home far into the course of the disorder.**

**Although there is no cure for Alzheimer's disease, treatments are available to alleviate many of the symptoms that cause suffering.**

A person with Alzheimer's disease may no longer be able to do math, but still be able to read a magazine with pleasure for months or years to come. Playing the piano might become too stressful in the face of increasing mistakes, but singing along with others may still be satisfying. The chess board may have to be put away, but one may still be able to play tennis. Thus, despite the many exasperating moments in the lives of Alzheimer patients and their families, many opportunities remain for positive interactions. Challenge, frustration, closeness, anger, warmth, sadness, and satisfaction may all be experienced by those who work to help the person with Alzheimer's disease cope as well as possible with the disease.

The reaction of an individual to the illness—his or her capacity to cope with it—also varies and may depend on such factors as lifelong personality patterns and the nature and severity of stress in the immediate environment. Depression, severe uneasiness, and paranoia or delusions may accompany or result from the disease, but they can often be alleviated by appropriate treatments. Although there is no cure for Alzheimer's disease, treatments are available to alleviate many of the symptoms that cause suffering.

## **The Diagnosis of Alzheimer's Disease**

### **Abnormal Brain Tissue Findings**

#### **1. Plaques and Tangles**

Microscopic brain tissue changes have been described in Alzheimer's disease since Alois Alzheimer first reported them in 1906. The two principal changes are senile or neuritic plaques (chemical deposits consisting of degenerating nerve cells combined with a form of protein called beta amyloid) and neurofibrillary tangles (malformations within nerve cells). The brains of Alzheimer's disease patients of all ages reveal these findings on autopsy examination.

The plaques found in the brains of people with Alzheimer's disease appear to be made, in part, from protein molecules—amyloid precursor protein (APP)—that normally are essential components of the brain. Plaques are made when an enzyme snips APP apart at a specific place and then leaves the fragments—beta amyloid—in brain tissue where they come together in abnormal deposits. It has not as yet been definitely determined how neurofibrillary tangles are formed.



As research on Alzheimer's disease progresses, scientists are describing other abnormal anatomical and chemical changes associated with the disease. These include nerve cell degeneration in the brain's nucleus basalis of Meynert and reduced levels of the neurotransmitter acetylcholine in the brains of Alzheimer's disease victims. But from a practical standpoint, the "classical" plaque and tangle changes seen in the brain at autopsy typically suffice for a diagnosis of Alzheimer's disease. In fact, it is still only through the study of brain tissue from a person who was thought to have Alzheimer's disease that a definitive diagnosis of the disorder can be made.

## 2. Brain Scans

Computer-Assisted Tomography (CAT scan) changes become more evident as the disease progresses—not necessarily early on. Thus a CAT scan performed in the first stages of the disease cannot in itself be used to make a definitive diagnosis of Alzheimer's disease; its value is in helping to establish whether certain disorders (some reversible) that mimic Alzheimer's disease are present. Later on, CAT scans often reveal changes characteristic of Alzheimer's disease, namely an atrophied (shrunken) brain with widened sulci (tissue indentations) and enlarged cerebral ventricles (fluid-filled chambers).

Several new types of instrumentation are enabling researchers to learn even more about the brain. Both positron emission tomography (PET scan) and SPECT (single photon emission computerized tomography) can map regional cerebral blood flow, metabolic activity, and distribution of specific receptors, as well as integrity of the blood-brain barrier. These procedures may reveal abnormalities characteristic of Alzheimer's disease. Another method, magnetic-resonance imaging (MRI), probes the brain by examining the interaction of the magnetic properties of atoms with an external magnetic field. MRI provides both structural and chemical information and distinguishes moving blood from static brain tissue (Taylor, 1990).

## Clinical Features of Alzheimer's disease

The "clinical" features of Alzheimer's disease, as opposed to the "tissue" changes, are threefold:

1. Dementia--significant loss of intellectual abilities such as memory capacity, severe enough to interfere with social or occupational functioning;
2. Insidious onset of symptoms--subtly progressive and irreversible course with documented deterioration over time;
3. Exclusion of all other specific causes of dementia by history, physical examination, laboratory tests, psychometric, and other studies.

## Diagnosis By Exclusion

Based on these criteria, the clinical diagnosis of Alzheimer's disease has been referred to as "a diagnosis by exclusion," and one that can only be made in the face of clinical deterioration over time. There is no specific clinical test or finding that is unique to Alzheimer's disease. Hence, all disorders that can bring on similar symptoms must be systematically excluded or "ruled out." This explains why diagnostic workups of individuals where the question of Alzheimer's disease has been raised can be so frustrating to patient and family alike; they are not told that Alzheimer's disease has been specifically diagnosed, but that other possible diagnoses have been dismissed, leaving Alzheimer's disease as the likely diagnosis by the process of elimination.

Some scientists think that the results from biochemical research may lead to a diagnostic "marker" for certain persons evaluated for Alzheimer's disease. For example, research has discovered a protein, called Alzheimer's Disease Associated Protein (ADAP), in the autopsied brains of Alzheimer's patients. The protein, which seems to appear only in people with Alzheimer's, is mainly concentrated in the cortex covering the front and side sections of the brain, regions involved in memory function. Researchers have found ADAP not only in brain tissue but also in spinal fluid. If they can perfect a test to detect the protein in the cerebrospinal fluid, or potentially even circulating in the blood, it may be possible to use this method of diagnosis on living patients.

Many scientists are working at developing other tests or procedures that may someday identify living persons with the disorder, perhaps even early in its course before

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behavioral changes become evident. Still, a reliable, specific diagnostic marker for Alzheimer's disease is not yet available.

Meanwhile, Alzheimer's disease is the most overdiagnosed and misdiagnosed disorder of mental functioning in older adults. Part of the problem, already alluded to, is that many other disorders show symptoms that resemble those of Alzheimer's disease. The crucial difference, though, is that many of these disorders—unlike Alzheimer's disease—may be stopped, reversed, or cured with appropriate treatment. But first they must be identified and not dismissed as Alzheimer's disease or senility.

Conditions that affect the brain and result in intellectual, behavioral, and psychological dysfunction are referred to as "organic mental disorders." These disorders represent a broad grouping of diseases and include Alzheimer's disease. Organic mental disorders that can cause clinical problems like those of Alzheimer's disease, but which might be reversible or controlled with proper diagnosis and treatment, include the following:

- **Side Effects of Medications:** Unusual reactions to medications, too much or too little of prescribed medications, combinations of medications which, when taken together, cause adverse side effects.
- **Substance Abuse:** Abuse of legal and/or illegal drugs, alcohol abuse.
- **Metabolic Disorders:** Thyroid problems, nutritional deficiencies, anemias, etc.
- **Circulatory Disorders:** Heart problems, strokes, etc.
- **Neurological Disorders:** Normal-pressure hydrocephalus, multiple sclerosis, etc.
- **Infections:** Especially viral or fungal infections of the brain.
- **Trauma:** Injuries to the head.
- **Toxic Factors:** Carbon monoxide, methyl alcohol, etc.
- **Tumors:** Any type within the skull—whether originating or metastasizing there.

In addition to organic mental disorders resulting from these diverse causes, other forms of mental dysfunction or mental health problems can also be confused with Alzheimer's disease. For example, severe forms of depression can cause problems with memory and concentration that initially may be indistinguishable from

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**Serious memory difficulties should not be dismissed as an unavoidable part of normal aging.**

early symptoms of Alzheimer's disease. Sometimes these conditions, referred to as "pseudodementia," can be reversed. Other psychiatric problems can similarly masquerade as Alzheimer's disease, and, like depression, respond to treatment.

Of course, not all memory changes or complaints in later life signal Alzheimer's disease or mental disorder. Many memory changes are only temporary, such as those that occur with bereavement or any stressful situation that makes it difficult to concentrate. In fact, older people are often accused or accuse themselves of memory changes which are not really taking place. If a person in his thirties misplaces keys or a wallet, forgets the name of a neighbor, or calls one sibling by another's name, nobody gives it a second thought. But the same normal forgetfulness for people in their seventies may raise unjustifiable concern. On the other hand, serious memory difficulties should not be dismissed as an unavoidable part of normal aging. Since rigorous studies on intelligence in later life show that healthy people who stay intellectually active maintain a sharp mind throughout the life cycle, noticeable decline in older adults that interferes with functioning should be clinically explored for an underlying problem.

## **The Importance of a Comprehensive Clinical Evaluation**

Because of the many other disorders that can be confused with Alzheimer's disease, a comprehensive clinical evaluation is essential to arrive at a correct diagnosis of symptoms that look like those of Alzheimer's disease. Such an assessment should include at least three major components—(1) a thorough general medical workup, (2) a neurological examination, and (3) a psychiatric evaluation that may include psychological or psychometric testing. The family physician can be consulted about the best way to get the necessary examinations.

**George tried to get Mary Ellen to see their family physician but she refused. Finally, he suggested that they both go in to have their blood pressure checked. The doctor was shocked at the deterioration in Mary Ellen's personality and scheduled a complete physical examination for her.**

He also made an appointment with a neurologist for further neurological examination, including a CAT scan. A psychiatrist working in the same office conducted a psychiatric evaluation. George helped by giving them many details of Mary Ellen's history. A tentative diagnosis of Alzheimer's disease was made, and George was instructed to bring Mary Ellen back in 6 months for further evaluation. George still hoped that Mary Ellen's condition was temporary and told no one of his distress. When their two daughters called, he always made excuses as to why their mother did not answer the telephone. He neglected his writing as more of his time was taken up with household tasks that Mary Ellen no longer even tried to do.

Alzheimer's disease has emerged as one of the great mysteries in modern day medicine, with a growing number of clues but still no answers as to its cause. The quest to uncover its cause has the air of a veritable whodunit saga. Though none of the leading theories about the genesis of Alzheimer's disease has resolved the mystery, each has led to certain intriguing findings that suggest further investigation is needed. It is important to examine these theories, not only to understand current thinking on Alzheimer's disease, but also to learn what popular ideas have proved to be incorrect. There have been at least five prominent theories about the cause of Alzheimer's disease:

## The Search for the Cause of Alzheimer's Disease

### 1. Chemical Theories (Deficiencies and Toxic Excesses)

#### *A. Biochemical Changes in Growth (Trophic)*

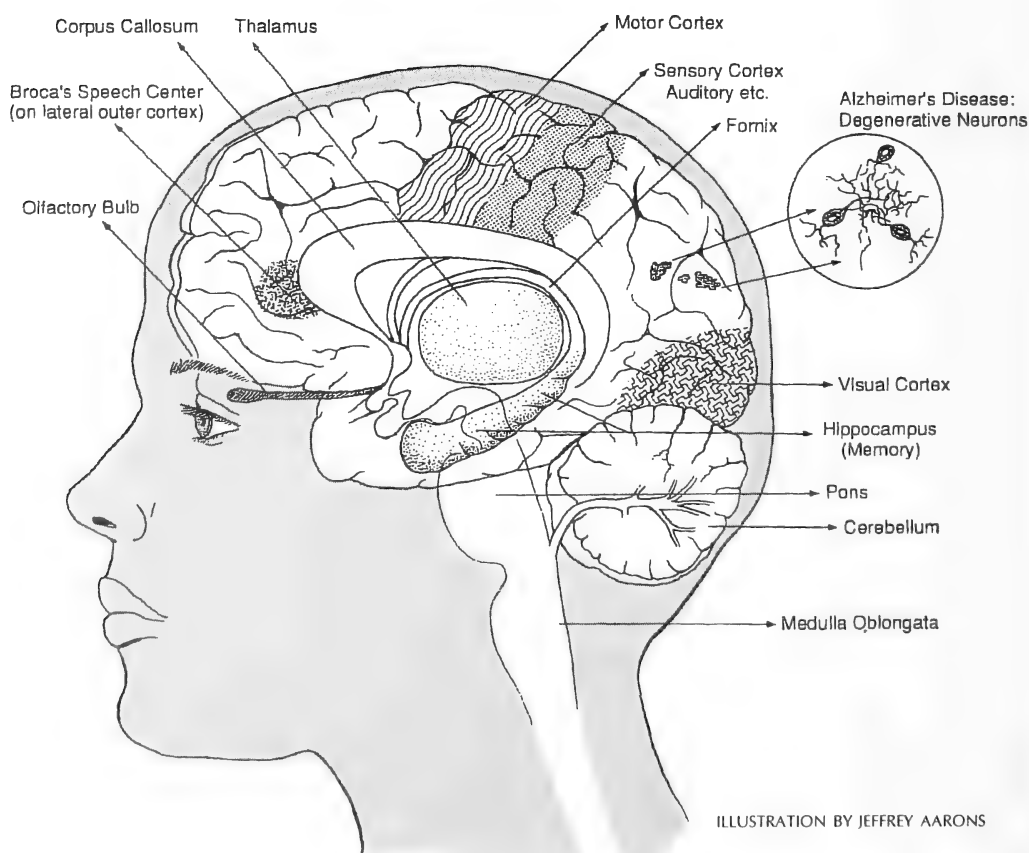
**Factors:** Much research is taking place in the examination of naturally occurring substances that may affect the nervous system and that may contribute to the dysfunction or death of brain cells in Alzheimer's. It is possible that one reason for nerve cell death in Alzheimer's patients is a decline in growth-promoting factors that maintain the functioning of brain cells, or, conversely, a spontaneous increase in factors that are toxic to brain cells.

A naturally occurring substance of interest is nerve growth factor (NGF). Experiments in aged rats indicate that specific nerve growth factors can stimulate the growth of new

synaptic connections in the hippocampus and, as a result, restore some memory loss. Although there could be neurotoxic as well as growth-enhancing effects in the use of NGF, scientists are investigating methods of safely introducing NGF into the brain, possibly through the transplant of genetically engineered cells.

Other research is exploring whether changes or an imbalance in the metabolism of certain elements like calcium in brain cells may be part of the process by which the cells degenerate and die in Alzheimer's disease.

**B. Chemical Deficiencies:** One of the ways in which brain cells communicate with one another is through chemicals called neurotransmitters. Studies of Alzheimer's disease brains have uncovered diminished levels of various neurotransmitters that are thought to influence intellectual



functioning and behavior. For example, reduced levels of the neurotransmitter acetylcholine (ACh) have been found in Alzheimer's disease. This finding has been coupled with observations that drugs whose side effects lower ACh levels in the brain can cause reversible memory problems. These findings have led to a number of drug studies employing pharmacologic agents to elevate ACh in patients. The treatments have included lecithin, choline, physostigmine, deprenyl, tacrine hydrochloride (THA), and others, used alone or in different combinations with one another. The results of these experiments are difficult to interpret. In some of these studies, a few Alzheimer's disease patients seem to show minor improvement over a brief but not sustained period of time. Typically, any improvement may be on certain narrow test measures--and not usually on significant activities of daily living which would be more important to the person's family and physician. Nonetheless, the researchers' enthusiasm is understandable, for they are dealing with the potential modifiability of underlying physiological phenomena that influence the Alzheimer's disease symptoms. The drugs they are studying now may not be the right ones, but they may point the way to the discovery of more effective pharmacologic agents.

One drug in particular, THA or tacrine (trade name, Cognex), has been studied extensively. Early studies indicated that THA appeared to have a slightly positive effect on patient functioning, but assessment by a skilled observer showed no overall improvement. More recent studies conducted on patients with mild or moderate Alzheimer's, using a higher dosage of tacrine than the earlier studies, showed a statistically significant improvement, both in clinical and caregiver evaluations and in quality of life measurements. These results caused the Food and Drug Administration in the fall of 1993 to approve the drug. Tacrine can, however, have side effects, including elevation of liver functioning tests. The family of the patient should be aware that the patient must take the medication 4 times a day, that blood must be drawn weekly during the dose adjustment phase, and that a third of patients experience significant adverse effects. As is always the case, but particularly while better drugs are being developed, caregivers and patients will have to weigh the possible benefits of the available drug against the cost and the potential problems incurred.

**C. Toxic Chemical Excesses:** Although some researchers have found increased levels of aluminum, mercury, or other metals in the brains of Alzheimer's disease victims, others have not. And while some investigators have hypothesized that aluminum may play a role in the genesis of Alzheimer's disease, most have regarded aluminum as an effect of the disorder rather than its cause. In other words, instead of aluminum's acting to induce brain tissue changes in Alzheimer's disease, it more likely accumulates in response to such changes. Research continues in an effort to better understand this phenomenon and to determine whether the aluminum deposits are a cause or a consequence of the disease, and, if the latter, whether they contribute further to the impairment already experienced.

## 2. The Genetic Theory

Genetic aspects of many diseases are confusing. For example, a disorder can occur more frequently in certain families than in others, but still not be genetic. Since family members living together are exposed to the same environment, they would all be at increased risk if an environmental toxin or infectious agent were the causative factor in a particular disease. Furthermore, a disorder can be congenital and not hereditary—that is, prenatal problems can cause developmental defects not brought on by heredity. And an illness can be hereditary but remain in a latent state if some other disease factor does not occur to trigger its onset.

Several connections between Alzheimer's disease and Down's syndrome led researchers initially to look for genetic factors in Alzheimer's disease on chromosome 21—the chromosome that is affected in Down's syndrome. At the present time, several genetic markers have been identified on chromosomes 21 and 14 in that small number of families where Alzheimer's disease has occurred with unusual frequency at relatively early ages. In families where the disease has tended to develop at later ages, other studies suggest that Alzheimer's disease is unusually frequent in persons who have a particular form of the apolipoprotein E (ApoE) gene found on chromosome 19. Only a minority of the general population show this version (ApoE4) of the gene, out of several variants that occur.

Despite these findings, the extent of genetic and hereditary involvement in Alzheimer's disease remains

The extent of genetic and hereditary involvement in Alzheimer's disease remains unclear.



unclear. There are a vast number of people affected with this disorder who are not part of a strong family pattern. Furthermore, the genetic factors associated with the disease clearly vary for different families. This has led some investigators to postulate that there may be a number of subtypes of Alzheimer's disease, with differing risk factors and causes.

The National Institute of Mental Health (NIMH) is supporting research to locate the genes that cause Alzheimer's disease, schizophrenia, and manic depression. Ten diagnostic centers, three of which study Alzheimer's, provide genetic material to a central gene bank. Scientists at the centers use identical diagnostic tests, chosen for their sensitivity and reliability, to select members of families whose blood is sent to the gene bank for processing, storage, and distribution. Participating families must have several members affected by one of the diseases. The centers studying Alzheimer's are: The Johns Hopkins University, Baltimore, Maryland; Massachusetts General Hospital, Boston, Massachusetts; and University of Alabama, Birmingham, Alabama.

### 3. The Autoimmune Theory

The body's immune system, which protects against potentially harmful foreign invaders, may erroneously begin to attack its own tissues, producing antibodies to its own essential cells. This is called an autoimmune response, and it may take place in the brain. Some scientists speculate that certain late life changes in aging neurons (the major nerve cells of the brain) might be triggering an autoimmune response that evokes symptoms of Alzheimer's disease in vulnerable individuals. Curiously, some antibrain antibodies have been identified in the brains of those with Alzheimer's disease. Their significance, though, is not known, especially since some antibrain antibodies have also been identified in aging brains without Alzheimer's disease. Moreover, even if changes are occurring in brain neurons to trigger an autoimmune response, what originally induces these brain cell changes is not known.

### 4. The Slow Virus Theory

Because a slow-acting virus has been identified as a cause of some brain disorders that closely resemble

Alzheimer's disease (for example, Creutzfeldt-Jakob disease), a slow virus has been postulated in Alzheimer's disease. Various researchers have suggested that suspicious brain tissue changes in Alzheimer's disease victims may be caused by a virus. However, to date a virus has not been isolated from the brains of those with Alzheimer's disease, and no immune reaction has been found in the brains of Alzheimer's patients, comparable to that found in patients with other viral dementias. At present, the possibility of a viral cause of Alzheimer's cannot be either decisively eliminated or confirmed.

## 5. The Blood Vessel Theory

Defects in blood vessels supplying blood to the brain have been studied as a possible cause of Alzheimer's disease. Hardening of the brain's arteries, also known as cerebroarteriosclerosis, proved not to be a cause of Alzheimer's disease. Thus, the hyperbaric oxygen chamber treatment proved ineffective as a therapy for Alzheimer's.

Stroke, another blood vessel problem that most often occurs later in life, can cause symptoms like those of Alzheimer's disease. But this condition, called multi-infarct dementia, differs from Alzheimer's disease. More recently, the blood vessel theory has been expanded to hypothesize potential defects in the blood-brain barrier, a protective membrane-like mechanism that guards the brain from foreign bodies or toxic agents circulating in the blood stream outside the brain.

There have been several reports of a possible association between serious head injuries involving a loss of consciousness and later onset of Alzheimer's disease. One theory as to why this connection might occur has to do with possible breaks in the blood-brain barrier as a result of these injuries to the brain.

Two critical crossroads reached in the approach to treatment for Alzheimer's disease were (1) the recognition of Alzheimer's disease as a disorder distinct from the normal aging process; and (2) the realization that, in developing therapeutic and social interventions for a major illness or disability, the concept of care can be as important as that of cure. Moreover, in addition to the symptoms of Alzheimer's disease mentioned earlier, other symptoms and aggravating factors may compound the problem. Patient, environmental, and family stresses can converge to exaggerate patient dysfunction and family burden during the clinical course of Alzheimer's disease. Identifying these stresses and making appropriate changes can provide the foundation for more effective treatment and fewer everyday problems.

In the Alzheimer's disease patient, depression or delusions can aggravate dysfunction. These problems, which emerge during the course of the disorder in some individuals with Alzheimer's disease, compound memory impairment; they make the affected individual do worse than would be expected from the dementia alone--causing clinical conditions referred to as "excess disability" states. Depression by itself can mimic dementia--a condition that is sometimes termed pseudodementia. When combined with dementia, depression exacts yet greater incapacity and suffering in the Alzheimer's disease patient. Depression in Alzheimer's disease can be treated. Indeed this highlights one of the truly extraordinary phenomena that can be observed in Alzheimer's disease: By alleviating an excess disability state, actual clinical improvement can result--even though the underlying disease process is advancing. In other words, at a given point in time, the patient's symptoms can be reduced, suffering lowered, capacity to cope buttressed, with family burden eased as a further result. These are traditional goals of treatment for all illnesses.

Researchers in the NIMH Intramural program have developed and are testing a Dementia Mood Assessment Scale, designed to rate mood in Alzheimer's patients. This scale tracks the mood states of the patients over the course of their illness and thus may be helpful in testing various antidepressant treatments.

The patient's immediate environment can also interfere with coping, adding to the level of impairment. Modifying the surroundings can reduce stresses imposed by

## The Treatment of Alzheimer's Disease

**In the Alzheimer's disease patient, depression or delusions can aggravate dysfunction.**

**Stress on the family can take a toll on patient and caregiver alike.**

environmental factors. There is the matter of safety, as in the need to protect the person from wandering toward a stairway and subsequently falling. There is the matter of lowering the individual's frustration level, such as by placing different cues in the immediate environment to combat memory loss and to reduce resulting stress and disorganization. There is the matter of finding the most protective but least restrictive setting for care which at some point may involve a move away from home to a nursing home or other care facility well equipped to deal with those who have Alzheimer's disease.

Stress on the family can take a toll on patient and caregiver alike. Caregivers are usually family members—either spouses or children—and are preponderantly wives and daughters. As time passes and the burden mounts, it not only places the mental health of family caregivers at risk, it also diminishes their ability to provide care to the Alzheimer's disease patient. Hence, assistance to the family as a whole must be considered.

As the disease progresses, families experience increasing anxiety and pain at seeing unsettling changes in a loved one, and they commonly feel guilt over not being able to do enough. The prevalence of reactive depression among family members in this situation is disturbingly high—caregivers are chronically stressed and are much more likely to suffer from depression than the average person. If caregivers have been forced to retire from positions outside the home, they feel progressively more isolated and no longer productive members of society.

An NIMH-funded study shows that caregivers not only have increased rates of infectious illness and depression, but often have suppressed immune systems. Another study of caregivers found depressed mood in 54 percent of caregivers and anger in 67 percent. Researchers hypothesize that the caregivers who hold in their anger may be at greater risk of cardiovascular disease.

The likelihood, intensity, and duration of depression among caregivers can all be lowered through available interventions. For example, to the extent that family members can offer emotional support to each other and perhaps seek professional consultation, they will be better prepared to help their loved one manage the illness and to recognize the limits of what they themselves can reasonably do.

George and Mary Ellen's neighbors had become increasingly concerned as it was obvious something was very wrong. When they noticed that the newspaper had not been taken in one morning, two neighbors came over. When no one answered the door, they tried it, found it unlocked, and entered. George was lying on the floor near the telephone, and Mary Ellen was sitting at the piano trying to pick out a tune. The neighbors called an ambulance for George and then placed a long-distance call to one of his daughters. George, in the hospital suffering from a heart attack, for the first time shared with his children the events of the past months and realized that he must make plans for the future. One of his daughters stayed with him and Mary Ellen for 2 months after he left the hospital. She arranged for someone to come in once a week to clean the house. She also contacted Meals-on-Wheels to ensure nourishing meals for her parents. Through her parents' church, she enrolled Mary Ellen in a 5-day-a-week daycare program for the elderly. Each morning Mary Ellen was picked up by the daycare van and was brought back late in the afternoon. George, relieved of constant anxiety, recovered rapidly and began to catch up on his writing projects. Though he missed the social life they had once enjoyed with their friends, there were times when he and Mary Ellen still felt a close relationship. George now accepted the fact that someday Mary Ellen might have to enter a nursing home, but with the support of his family, friends, church, and community he would be able to deal with whatever came.

Caregivers are chronically stressed and are much more likely to suffer from depression than the average person.

Since the components of the problem vary, so too should the focus, nature, and sources of interventions. Interventions should focus on the patient's symptoms, the affected individual's everyday environment, and the family support system. Specific interventions can involve support from the family, the help of a homemaker or other aide in the home, employment of behavioral therapies, and the use of medication. The sources for interventions can range from family support groups such as those available through the Alzheimer's Association (AA), to professional consultations for

the patient and family with a mental health specialist, to a variety of community programs such as day or respite care. Information on what assistance is available in a given community can be gained by contacting the local Office on Aging, a Community Mental Health Center or local Medical Society, or a local chapter of the AA. In addition, every State has an agency on aging that provides information on services and programs. The State Agencies on Aging, along with other sources of help, are listed at the back of this brochure.

Though Alzheimer's disease cannot at present be cured, reversed, or stopped in its progression, much can be done to help both the patient and the family live through the course of the illness with greater dignity and less discomfort. Toward this goal, appropriate clinical interventions and community services should be vigorously sought.

## Hope for the Future Through Research

**There is considerable excitement and hope about new findings that are unfolding in numerous research settings.**

While Alzheimer's disease remains a mystery, with its cause and cure not yet found, there is considerable excitement and hope about new findings that are unfolding in numerous research settings. The connecting pieces to the puzzle called Alzheimer's disease continue to be found. At the same time, there are more and more partners involved in the effort, with growing national and international interest. Government, industry, academia, and the volunteer sector are all becoming more and more active; Federal, State, community, corporate, and foundation support for new studies and better services are all on the rise.

The U.S. Department of Health and Human Services established a Departmental Task Force on Alzheimer's Disease, which first met in April 1983. This Task Force, later legislatively mandated as the Council on Alzheimer's Disease, is composed of representatives from the following agencies that have programs related to Alzheimer's disease: the National Institute of Mental Health, the National Institute on Aging, the National Institute of Neurological Disorders and Stroke, the National Institute of Allergy and Infectious Diseases, the National Institute for Nursing Research, the Administration on Aging, the Agency for Health Care Policy and Research, the Health Care Financing Administration, the Health Resources and Services Administration, the National Center for Health Statistics, and the Department of Veterans Affairs. The Council, which also includes both the Surgeon General and the Assistant Secretary for Planning and

Evaluation as members, is chaired by the Assistant Secretary for Health. The Council's recommendations are sent in an annual report to Congress.

In addition, a non-Federal Advisory Panel on Alzheimer's Disease was established by congressional action. The Panel, which works closely with the Council, consists of 15 national authorities on Alzheimer's disease selected for their depth and breadth of expertise in this area. The Panel has issued four reports, for 1988-89, 1990, 1991, and 1992. The titles are in the reference list. The activities of both the Council and the Panel reflect the scope of concern and interest that is being focused by the Federal Government on Alzheimer's disease.

**Acetylcholine** - a neurotransmitter found in reduced levels in the brains of Alzheimer's victims.

## Glossary

**Alzheimer's Disease Associated Protein (ADAP)** - a protein that seems to appear only in the tissue of people with Alzheimer's. It has been found in both the brain and spinal fluid.

**Amyloid precursor protein (APP)** - a normal, essential substance made by brain cells that contain **beta amyloid**. In Alzheimer's, APP is cut and releases beta amyloid. Beta amyloid then forms clumps called **senile plaque**.

**Apolipoprotein E (ApoE)** - a protein that ferries cholesterol through the bloodstream. The ApoE gene has three variants (or alleles), E2, E3, and E4. Each person inherits an allele from each parent. Ninety percent of the population inherit one copy of ApoE3, and 60 percent inherit two copies.

**Cortisol** - the major natural **glucocorticoid (GC)** in humans. It is the primary stress hormone.

**Dementia** - significant loss of intellectual abilities such as memory capacity, severe enough to interfere with social or occupational functioning.

**Hippocampus** - an area buried deep in the forebrain that helps regulate emotion and memory.

**Multi-Infarct Dementia** - dementia brought on by a series of strokes.

**Nerve Growth Factor** - a substance that occurs naturally in the body and enhances the growth and survival of cholinergic nerves.

**Neurotoxic** - poisonous to nerves or nerve tissue.

**Nucleus basalis of Meynert** - A small group of cholinergic nerve cells in the forebrain and connected to areas of the cerebral cortex.

**Pseudodementia** - a severe form of depression resulting from a progressive brain disorder in which cognitive changes mimic those of dementia.

## References

Advisory Panel on Alzheimer's Disease. Report of the Advisory Panel on Alzheimer's Disease. DHHS Pub. No. (ADM) 89-1644, Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1989. (Available from the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, GPO S/N 017-024-01387-1, \$2.25.)

Advisory Panel on Alzheimer's Disease. Second Report of the Advisory Panel on Alzheimer's Disease, 1990. DHHS Pub. No. (ADM) 91-1791, Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1991. (Available from the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, GPO S/N 017-024-01442-7, \$3.00.)

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Advisory Panel on Alzheimer's Disease. Fourth Report of the Advisory Panel on Alzheimer's Disease, 1992. NIH Pub. No. (NIH) 93-3520, Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1993. (Available from the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, GPO S/N 017-024-01508-3, \$3.75.)

Light, E., and Lebowitz, B.D. Alzheimer's Disease Treatment and Family Stress: Directions for Research. DHHS Pub. No. (ADM) 89-1569, Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1989. (Available from the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, GPO S/N 017-024-01365-0, \$14.00.)

National Institute of Mental Health. If You're Over 65 and Feeling Depressed . . . Treatment Brings New Hope. DHHS Pub. No. (ADM) 90-1653, 1990. (Single copies available from Public Inquiries, NIMH, 5600 Fishers Lane, Room 7C-02, Rockville, MD 20857. Available in packages of 50 from the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, GPO S/N 017-024-01376-5, \$23.00 per package of 50.)

National Institute of Mental Health. Plain Talk About Mutual Help Groups. DHHS Pub. No. (ADM) 89-1138, 1989. (Single copies available from Public Inquiries, NIMH, 5600 Fishers Lane, Room 7C-02, Rockville, MD 20857.)

Taylor, Rob. Evolutions: Brain imaging, The Journal of NIH Research, May 1990, Vol. 2, p. 103.

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U.S. Congress, Office of Technology Assessment. Summary, Confused Minds, Burdened Families: Finding Help for People with Alzheimer's and Other Dementias, OTA-BA-404, Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1990.

# Sources of Help

## State Agencies on Aging

\* In-State Toll-Free Number

These agencies coordinate services for older Americans, providing information on services, programs, and opportunities.

### ALABAMA

Executive Director  
Alabama Commission on Aging  
770 Washington Avenue, Suite 470  
RSA Plaza  
Montgomery, Alabama 36130  
(205) 242-5743

### ALASKA

Executive Director  
Older Alaskans Commission  
P.O. Box 110209  
Juneau, Alaska 99811-0209  
(907) 465-3250

### AMERICAN SAMOA

Director  
Territorial Administration on Aging  
Government of American Samoa  
Pago Pago, American Samoa 96799  
(684) 633-1251

### ARIZONA

Administrator  
Aging and Adult Administration  
Department of Economic Security  
1789 West Jefferson - 950A  
Phoenix, Arizona 85007  
(602) 542-4446  
\*1-(800) 352-3792

### ARKANSAS

Director  
Division of Aging and Adult Services  
Arkansas Department of Human Services  
1417 Donaghey Plaza South  
P.O. Box 1437, Slot 1412  
Little Rock, Arkansas 72201-1437  
(501) 682-2441

CALIFORNIA

Director

California Department of Aging

1600 K Street

Sacramento, California 95814

(916) 322-5290

COLORADO

Director

Aging and Adult Services

Department of Social Services

1575 Sherman Street, 10th Floor

Denver, Colorado 80203-1714

(303) 866-5905

COMMONWEALTH OF THE  
NORTHERN MARIANA ISLANDS

Administrator

Office on Aging

Department of Community and Cultural Affairs

Civic Center

Commonwealth of the Northern Mariana Islands

Saipan, Mariana Islands 96950

(670) 234-6011

CONNECTICUT

Director

Division of Elderly Services

Department of Social Services

175 Main Street

Hartford, Connecticut 06106

(203) 566-3238

\*1-(800) 443-9946

DELAWARE

Director

Delaware Division on Aging

Department of Health and Social Services

1901 North Dupont Highway - Second Floor

New Castle, Delaware 19720

(302) 577-4791

\*1-(800) 223-9074

DISTRICT OF COLUMBIA

Director

District of Columbia Office on Aging

Executive Office of the Mayor

441 - 4th Street, N.W., 9th Floor - South

Washington, D.C. 20001

(202) 724-5622

FLORIDA

Secretary

Florida Department of Elder Affairs

Building 1 - Room 317

1317 Winewood Boulevard

Tallahassee, Florida 32399-0700

(904) 922-5297

\*1-(800) 342-0825

GEORGIA

Director

Division of Aging Services

Department of Human Resources

2 Peachtree Street, N.E., 18th Floor

Atlanta, Georgia 30303

(404) 657-5258

GUAM

Administrator

Division of Senior Citizens

Department of Public Health and Social Services

P.O. Box 2816

Government of Guam

Agana, Guam 96910

(671) 734-2942

HAWAII

Executive Director

Hawaii Executive Office on Aging

335 Merchant Street, Room 241

Honolulu, Hawaii 96813

(808) 548-0100

IDAHO

Director

Idaho Office on Aging

Statehouse, Room 108

Boise, Idaho 83720

(208) 334-3833

ILLINOIS

Director

Illinois Department of Aging

421 East Capitol Avenue

Springfield, Illinois 62701

(217) 785-2870

\*1-(800) 252-8966

INDIANA

Commissioner

Indiana Department of Human Services

420 W. Washington Street

P.O. Box 7083

Indianapolis, Indiana 46207-7083

(317) 232-9020

\*1-(800) 545-7763

IOWA

Executive Director

Department of Elder Affairs

Jewett Building, Suite 236

914 Grand Avenue

Des Moines, Iowa 50309

(515) 281-5187

\*1-(800) 532-3213

KANSAS

Secretary

Kansas Department of Aging

Docking State Office Building, 150-S

915 S.W. Harrison

Topeka, Kansas 66612-1500

(913) 296-4986

\*1-(800) 432-3535

# KENTUCKY

Director  
 Division for Aging Services  
 Cabinet for Human Resources  
 Department for Social Services  
 275 East Main Street  
 Frankfort, Kentucky 40621  
 (502) 564-6930

# LOUISIANA

Director  
 Governor's Office of Elderly Affairs  
 4550 N. Boulevard  
 P.O. Box 80374  
 Baton Rouge, Louisiana 70806  
 (504) 925-1700

# MAINE

Director  
 Bureau of Elder and Adult Services  
 Department of Human Services  
 State House - Station 11  
 Augusta, Maine 04333  
 (207) 626-5335

# MARYLAND

Director  
 Maryland Office on Aging  
 301 West Preston Street  
 Baltimore, Maryland 21201  
 (301) 225-1102  
 \*1-(800) 338-0153

# MASSACHUSETTS

Secretary  
 Massachusetts Executive Office of Elder Affairs  
 1 Ashburton Place, 5th Floor  
 Boston, Massachusetts 02108  
 (617) 727-7750  
 \*1-(800) 882-2003

MICHIGAN

Director

Office of Services to the Aging

P.O. Box 30026

Lansing, Michigan 48909

(517) 373-8230

MINNESOTA

Executive Secretary

Minnesota Board on Aging

444 Lafayette Road, 4th Floor

St. Paul, Minnesota 55155-3843

(612) 296-2770

\*1-(800) 652-9747

MISSISSIPPI

Director

Division on Aging and Adult Services

Department of Human Resources

750 N. State Street

Jackson, Mississippi 39202

(601) 359-4925

\*1-(800) 222-7622

MISSOURI

Director

Division of Aging

Department of Social Services

615 Howerton Court

Jefferson City, Missouri 65102-1337

(314) 751-3082

\*1-(800) 235-5503

MONTANA

Coordinator

Governor's Office of Aging

Capitol Station, Room 219

P.O. Box 8005

Helena, Montana 59604

(406) 444-5900

\*1-(800) 332-2272

NEBRASKA

Director

Department on Aging

301 Centennial Mall South

P.O. Box 95044

Lincoln, Nebraska 68509-5044

(402) 471-2306

NEVADA

Administrator

Division for Aging Services

340 N. 11th Street, Suite 114

Las Vegas, Nevada 89158

(702) 486-3545

NEW HAMPSHIRE

Director

Division of Elderly and Adult Services

New Hampshire Department of Health and Human Services

115 Pleasant Street

Concord, New Hampshire 03301

(603) 271-4394

\*1-(800) 852-3345

NEW JERSEY

Director

New Jersey Division on Aging

Department of Community Affairs

101 South Broad Street - CN 807

Trenton, New Jersey 08625-0807

(609) 292-0920

\*1-(800) 792-8820

NEW MEXICO

Director

New Mexico State Agency on Aging

La Villa Rivera Building, Ground Floor

224 East Palace Avenue

Santa Fe, New Mexico 87501

(505) 827-7640

\*1-(800) 432-2080



NEW YORK

Director

New York State Office for the Aging  
 Agency Building #2, Empire State Plaza  
 Albany, New York 12223-0001  
 (518) 474-5731  
 \*1-(800) 342-9871

NORTH CAROLINA

Director

North Carolina Division on Aging  
 Department of Human Resources, Kirby Building  
 639 Palmer Drive, Caller Box 29531  
 Raleigh, North Carolina 27626-0531  
 (919) 733-3983  
 \*1-(800) 622-7030

NORTH DAKOTA

Director

Aging Services Division  
 North Dakota Department of Human Services  
 1929 N. Washington Street  
 P.O. Box 7070  
 Bismarck, North Dakota 58507-7070  
 (701) 224-2577  
 \*1-(800) 472-2622

OHIO

Director

Ohio Department of Aging  
 50 West Broad Street - 9th Floor  
 Columbus, Ohio 43215  
 (614) 466-5500

OKLAHOMA

Division Administrator

Aging Services Division  
 Department of Human Services  
 312 N.E. 28th Street  
 P.O. Box 25352  
 Oklahoma City, Oklahoma 73125  
 (405) 521-2327

OREGON

Administrator  
 Senior and Disabled Services Division  
 Department of Human Resources  
 500 Summer Street, N.E., 2nd Floor  
 Salem, Oregon 97310-1015  
 (503) 378-4728

PENNSYLVANIA

Secretary  
 Pennsylvania Department of Aging  
 400 Market Street, 6th Floor, MSSOB  
 Harrisburg, Pennsylvania 17101-2301  
 (717) 783-1550

PUERTO RICO

Executive Director  
 Puerto Rico Office of Elderly Affairs  
 Call Box 50063  
 Old San Juan Station, Puerto Rico 00902  
 (809) 721-0753

REPUBLIC OF PALAU

Director  
 State Agency on Aging  
 Department of Social Services  
 Republic of Palau  
 Koror, Palau 96940

RHODE ISLAND

Director  
 Department of Elderly Affairs  
 160 Pine Street  
 Providence, Rhode Island 02903  
 (401) 277-2858  
 \*1-(800) 322-2880

SOUTH CAROLINA

Executive Director  
 South Carolina Division on Aging  
 202 Arbor Lake Drive  
 Suite 301  
 Columbia, South Carolina 29223-4535  
 (803) 737-7500  
 \*1-(800) 922-1107

SOUTH DAKOTA

Administrator  
Office of Adult Services and Aging  
Richard F. Kneip Building  
700 Governors Drive  
Pierre, South Dakota 57501-2291  
(605) 773-3656

TENNESSEE

Executive Director  
Tennessee Commission on Aging  
706 Church Street  
Suite 201  
Nashville, Tennessee 37243-0860  
(615) 741-2056

TEXAS

Executive Director  
Texas Department on Aging  
1949 - 1H 35 South  
P.O. Box 12786  
Capitol Station  
Austin, Texas 78711  
(512) 444-2727  
\*1-(800) 252-9240

UTAH

Director  
Utah Division of Aging & Adult Services  
120 North 200 West, Room 401  
P.O. Box 45500  
Salt Lake City, Utah 84145-0500  
(801) 538-3910

VERMONT

Commissioner  
Department of Rehabilitation and Aging  
103 S. Main Street  
Waterbury, Vermont 05671-2301  
(802) 241-2400  
\*1-(800) 642-5119

VIRGIN ISLANDS

Commissioner

Virgin Islands Department of Human Services

Knud Hansen Complex, Building A

1303 Hospital Ground

Charlotte Amalie, Virgin Islands 00840

(809) 774-1166

VIRGINIA

Commissioner

Virginia Department for the Aging

700 East Franklin Street - 10th Floor

Richmond, Virginia 23219-2327

(804) 225-2271

\*1-(800) 552-3402

WASHINGTON

Assistant Secretary

Aging and Adult Services Administration

Department of Social and Health Services

P.O. Box 45050

Olympia, Washington 98504-5050

(206) 586-3768

\*1-(800) 422-3263

WEST VIRGINIA

Director

West Virginia Office of Aging

State Capitol Complex - Holly Grove

1900 Kanawha Boulevard

Charleston, West Virginia 25305-0160

(304) 558-3317

\*1-(800) 642-3671

WISCONSIN

Director

Bureau on Aging

Department of Health and Social Services

217 S. Hamilton, Suite 300

Madison, Wisconsin 53707

(608) 266-2536

WYOMING

Administrator

Commission on Aging

Hathaway Building, Room 139

Cheyenne, Wyoming 82002

(307) 777-7986

**Alzheimer's Association, Inc.**

919 North Michigan Ave., Suite 1000

Chicago, Illinois 60611

Telephone: (312) 335-8700

Toll Free: (Illinois) 1-800-272-3900

(National) 1-800-621-0379

(Provides support through AA Chapter Family Support Groups; educational and patient care materials; information about local resources and services)

**Alzheimer's Disease Education and Referral Center**

P.O. Box 8250

Silver Spring, Maryland 20907-8250

Telephone: (301) 495-3311

Toll Free: 1-800-438-4380

(A service of the National Institute on Aging, the center distributes information on Alzheimer's disease, on current research activities, and on services available to patients and family members)

This is the second revision of the brochure by Margaret Strock, staff member in the Information Resources and Inquiries Branch, Office of Scientific Information, National Institute of Mental Health (NIMH). Expert assistance was provided by Barry D. Lebowitz, Ph.D., George T. Niederehe, Ph.D., Jane L. Pearson, Ph.D., Benjamin Wolozin, M.D., Ph.D., and Trey Sunderland, M.D., NIMH staff members. Their help in assuring the accuracy of this pamphlet is gratefully acknowledged. An earlier version of the brochure was written by Gene D. Cohen, M.D., Ph.D., former Director of the NIMH Program on Aging, in 1987. It was printed as a cooperative public-private effort by the American Association for Geriatric Psychiatry.

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